

**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference Case 21147	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP 03/01537	International filing date (day/month/year) 15.02.2003	Priority date (day/month/year) 22.02.2002
International Patent Classification (IPC) or both national classification and IPC C12P7/26		
Applicant DSM IP ASSETS B.V. et al.		

<p>1. This International preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the opinion</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>

Date of submission of the demand  24.07.2003	Date of completion of this report  05.02.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer  Devijver, K  Telephone No. +31 70 340-4124

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No.

PCT/EP 03/01537

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-10                                  as originally filed

**Claims, Numbers**

1-18                                  as originally filed

**Sequence listing part of the description, pages:**

1-5, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description,        pages:
- the claims,           Nos.:
- the drawings,        sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

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**6. Additional observations, if necessary:**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	
	No: Claims	1-18
Inventive step (IS)	Yes: Claims	
	No: Claims	1-18
Industrial applicability (IA)	Yes: Claims	1-18
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

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**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. CITATIONS**

**1.1 Reference is made to the following documents:**

D1: VAZ ALFIN D N ET AL: 'Old yellow enzyme: Aromatization of cyclic enones and the mechanism of a novel dismutation reaction.' BIOCHEMISTRY, vol. 34, no. 13, 1995, pages 4246-4256, XP001164161 ISSN: 0006-2960

**2. NOVELTY (Art. 33(2) PCT)**

- 2.1 The present application does not satisfy the criterion set forth in Article 33(2) PCT, because the subject-matter of claims 1-18 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).
- 2.2 Document D1 (the whole document) discloses the NADPH-dependent reduction of the olefinic bond of alpha,beta-unsaturated carbonyl compounds (reaction in general, see figure 1 and page 4250 right-hand column paragraph 3 - page 4251 right-hand column paragraph 2), e.g. ketoisophorone (= 2,6,6-trimethylcyclohex-2-ene-1,4-dione, see table 1), by old yellow enzyme isolated from Brewer's Bottom Yeast (*Saccharomyces carlsbergensis*) or from *Escherichia coli* recombinantly expressing OYE1, OYE2 or OYE3 (from *S. cerevisiae*) (cf. page 4247). The process was performed in the presence of NADPH at pH 7.0 and at 25°C (cf. table 1). Claims 1-18 lack novelty, because although D1 does not explicitly mention that levodione is produced, it is implicit in the sense that, in carrying out the teaching of D1, the skilled person would inevitably arrive at the result falling within the terms of the claims, since the starting products and the process of production are identical (PCT Guidelines, C-IV, 7.5).

It does not appear that the expression "S288C" or "ATCC 204508", relating to *S. cerevisiae* strains from which the old yellow enzyme is obtainable, imparts any

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distinguishing technical feature to the subject-matter of claims 6, 7 and 15. Therefore, D1 also anticipates the subject-matter of said claims.

**3. INVENTIVE STEP (Art. 33(3) PCT)**

- 3.1 The present application does not meet the requirements of Article 33(3) PCT, because the subject-matter of claims 1-18 does not involve an inventive step in the sense of Article 33(3) PCT.
- 3.2 Even if novelty could be established for claims 6, 7 and 15, it appears that these claims merely state a further *S. cerevisiae* strain, namely *S. cerevisiae* S288C (ATCC 204508), from which the old yellow enzyme NADPH dehydrogenase is obtainable. Lacking any unexpected effect linked to the use of *S. cerevisiae* S288C (ATCC 204508) for obtaining old yellow enzyme NADPH dehydrogenase, said claims are considered to lack an inventive step.

**4. FURTHER REMARKS**

- 4.1 There is no sufficient support (Art. 6 PCT) and no sufficient disclosure (Art. 5 PCT) for any process for producing levodione from ketoisophorone which comprises contacting ketoisophorone with NADPH dehydrogenase as such as referred to in claims 1-9, because the application does not disclose the use of NADPH dehydrogenase, being purified/isolated to a certain extent, in such a process. The application only provides support (Art. 6 PCT) and disclosure (Art. 5 PCT) for such a process which comprises contacting ketoisophorone with a (transformed) microorganism expressing NADPH dehydrogenase or a cell-free extract thereof (see examples 1-3).
- 4.2 The wording "derived", used in claims 7, 14 and 15, should be replaced by the wording "derivable". Claims 2 and 12 contain a typographical error, namely "EC 1.6.99.", which should be "EC 1.6.99.1."
- 4.3 Independent claim 18 does not contain any (essential) technical feature and hence, it does not meet the requirement following from Article 6 PCT taken in

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combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.